provisional application number 60/263,416, filed January 22, 2001. The disclosures of International application PCT/US02/01797 and United States provisional application 60/263,416 are incorporated by reference herein.

IN THE CLAIMS

Please cancel claims 2-33.

Please amend claim 1 as follows:*

1. (Amended) A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a first viral vector which comprises a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent is a second viral vector that does not comprise said therapeutic nucleic acid.

Please add claims 34-53 as follows:

34. (Added) A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent

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*Applicants attach Appendix B, which shows where changes in the claims have been made. Underlines indicate additions. Brackets indicate deletions.

is administered less than 1 hour prior to administering said viral vector.

35. (Added) The method according to claim 34, wherein said agent is administered less than five minutes prior to administering said viral vector.

36. (Added) A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent is administered concurrently with the viral vector.

37. (Added) A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent is a particle sufficient for phagocytosis and has a diameter of about 10 nm to about 1000 nm.

38. (Added) The method according to claim 1, wherein said first and/or second viral vector is an adenovirus vector.

39. (Added) The method according to any one of claims 34-38, wherein said viral vector is an adenovirus vector.

40. (Added) The method according to claim 1, wherein said subject is a rodent.

41. (Added) The method according to any one of claims 1 or 34-38, wherein said subject is a primate.

42. (Added) The method according to claim 41, wherein said primate is a human.

43. (Added) The method according to claim 1, wherein said first viral vector is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, topical administration, intraocular administration, intrabronchial administration, intraperitoneal administration, direct injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular delivery.

44. (Added) The method according to any one of claims 34-37, wherein said viral vector is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, topical administration, intraocular administration, intrabronchial administration, intraperitoneal administration, direct injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular delivery.

45. (Added) The method according to any one of claims 1, 34-37, wherein said agent is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, topical administration, intraocular administration, intrabronchial, intraperitoneal administration, direct injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular delivery.

46. (Added) The method according to any one of claims 34-37, wherein said viral vector is a replication-defective viral vector.

47. (Added) A method of modulating toxicity associated with a virally encoded transgene, the method comprising administering to a subject an agent that modulates Kupffer cell level or Kupffer cell function in said subject.

48. (Added) The method according to claim 47, wherein said agent is administered prior to administration of a therapeutic nucleic acid encoding a therapeutic gene product.

49. (Added) The method according to claim 47, wherein said toxicity is hepatotoxicity.

50. (Added) A method for modulating delivery of a virally encoded transgene to a subject, the method

comprising:

(a) identifying a dosage inflection point of a virus containing said virally encoded transgene in said subject;

(b) comparing said inflection point to levels of a product of said virally encoded transgene in said subject; and

(c) adjusting if necessary the dose of virus administered to said subject, thereby modulating dosage of said virally encoded transgene.

51. (Added) A method for modulating delivery of a virally encoded transgene to a subject, the method comprising:

(a) identifying a first dosage inflection point of a first virus not containing said encoded transgene in said subject, thereby saturating a Kupffer cell function;

(b) identifying a second dosage inflection point of a second virus containing said virally encoded transgene in said subject, wherein the dosage curve is non-linear;

(c) comparing said second inflection point to levels of a product of said virally encoded transgene in said subject; and

(d) adjusting if necessary the doses of the first virus and second virus administered to said